

compounds that may be used in the *methods* of the present invention, as described in this section of the specification, does not contain the provisos set forth in the section of the specification on pages 20 to 26, that is directed specifically to *compounds*. The provisos were included in the latter section, because certain species covered by the generic disclosure had been described previously. However, the use of such compounds in the methods defined by the pending claims was neither taught nor suggested in that art. Accordingly, the genus of compounds suitable in the claimed methods, as described at pages 14 to 20, is broader than the genus of novel compounds, described at pages 20 to 26.

Applicants respectfully submit that the full scope of the invention, as defined by the pending claims, is described in the specification, as required by 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Copies of the references cited in the IDS submitted on August 16, 2001 are enclosed herewith. Consideration of the references is respectfully requested.

Applicants acknowledge the non-statutory double patenting rejection over Claims 28 and 29 of co-owned U.S. Patent No. 6,191,131. Applicants propose to file a terminal disclaimer to overcome this rejection upon receiving an indication from the Examiner that the claims otherwise define allowable subject matter.

If there are any additional issues, or if the Examiner wishes to discuss this application further, please telephone the Applicants' undersigned representative at the telephone number below. Applicants note, however, that all written correspondence for this application should continue to be sent to:

Bristol-Myers Squibb Pharma Company  
Patent Department  
PO Box 4000  
Route 206 and Provinceline Road  
Princeton, NJ 08453-4000

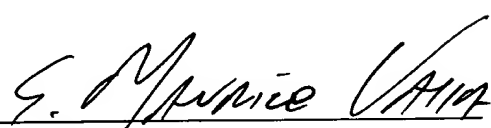
DOCKET NO.: BMS-0826/DM-6864-F - 7 -

PATENT

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Date:

2/21/03

  
S. Maurice Valla

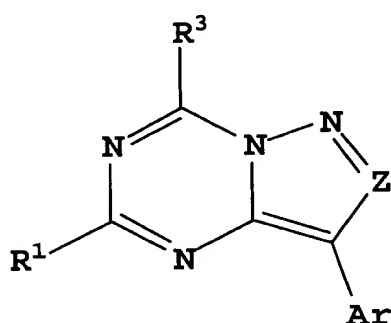
Registration No. 43,966

Woodcock Washburn LLP  
One Liberty Place - 46th Floor  
Philadelphia PA 19103  
Telephone: (215) 568-3100  
Facsimile: (215) 568-3439

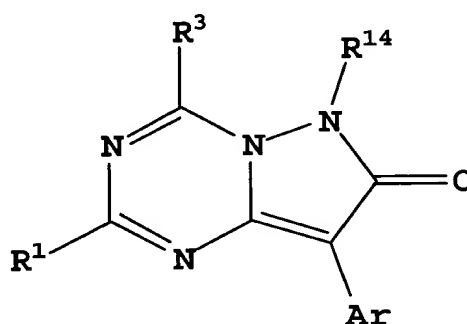
**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Claim 1 has been re-typed, as follows:

1. A method of treating a disorder induced or facilitated by CRF in a mammal comprising administering to said mammal a therapeutically effective amount of a compound of Formulae (1) or (2):



(1)



(2)

isomers thereof, stereoisomeric forms thereof, mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt forms thereof, wherein:

$Z$  is  $CR^2$ ;

$Ar$  is selected from phenyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, furanyl, thienyl, benzothienyl, benzofuranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-benzopyranyl, tetralinyl, each  $Ar$  optionally substituted with 1 to 5  $R^4$  groups and each  $Ar$  is attached to an unsaturated carbon atom;

$R^1$  is independently selected at each occurrence from H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>2</sub>-C<sub>4</sub> alkynyl, halo, CN, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>1</sub>-C<sub>12</sub> hydroxyalkyl, C<sub>2</sub>-C<sub>12</sub> alkoxyalkyl, C<sub>2</sub>-C<sub>10</sub> cyanoalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl,  $NR^9R^{10}$ , C<sub>1</sub>-C<sub>4</sub> alkyl- $NR^9R^{10}$ ,  $NR^9COR^{10}$ ,  $OR^{11}$ , SH or  $S(O)_nR^{12}$ ;

$R^2$  is selected from H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>2</sub>-C<sub>4</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl,

C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl, C<sub>1</sub>-C<sub>4</sub> hydroxyalkyl, halo, CN, -NR<sup>6</sup>R<sup>7</sup>, NR<sup>9</sup>COR<sup>10</sup>, -NR<sup>6</sup>S(O)<sub>n</sub>R<sup>7</sup>, S(O)<sub>n</sub>NR<sup>6</sup>R<sup>7</sup>, C<sub>1</sub>-C<sub>4</sub> haloalkyl, -OR<sup>7</sup>, SH or -S(O)<sub>n</sub>R<sup>12</sup>;

R<sup>3</sup> is selected from:

-H, SH, S(O)<sub>n</sub>R<sup>13</sup>, COR<sup>7</sup>, CO<sub>2</sub>R<sup>7</sup>, OC(O)R<sup>13</sup>, NR<sup>8</sup>COR<sup>7</sup>, N(COR<sup>7</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>13</sup>, N(OR<sup>7</sup>)R<sup>6</sup>, CONR<sup>6</sup>R<sup>7</sup>, aryl, heteroaryl and heterocycle, or  
 -C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>5</sub>-C<sub>8</sub> cycloalkenyl, C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl or C<sub>6</sub>-C<sub>10</sub> cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>13</sup>, COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>13</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>13</sup>, NR<sup>16</sup>R<sup>15</sup>, CONR<sup>16</sup>R<sup>15</sup>, aryl, heteroaryl and heterocyclyl;

R<sup>4</sup> is independently selected at each occurrence from: C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl, NO<sub>2</sub>, halo, CN, C<sub>1</sub>-C<sub>4</sub> haloalkyl, NR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>COR<sup>7</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>7</sup>, COR<sup>7</sup>, OR<sup>7</sup>, CONR<sup>6</sup>R<sup>7</sup>, CO(NOR<sup>9</sup>)R<sup>7</sup>, CO<sub>2</sub>R<sup>7</sup>, or S(O)<sub>n</sub>R<sup>7</sup>, where each such C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl and C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl are optionally substituted with 1 to 3 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>4</sub> alkyl, NO<sub>2</sub>, halo, CN, NR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>COR<sup>7</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>7</sup>, COR<sup>7</sup> OR<sup>7</sup>, CONR<sup>6</sup>R<sup>7</sup>, CO<sub>2</sub>R<sup>7</sup>, CO(NOR<sup>9</sup>)R<sup>7</sup>, or S(O)<sub>n</sub>R<sup>7</sup>;

R<sup>6</sup>, R<sup>7</sup>, R<sup>6a</sup> and R<sup>7a</sup> are independently selected at each occurrence from:

-H,  
 -C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> alkenyl, C<sub>3</sub>-C<sub>10</sub> alkynyl, C<sub>1</sub>-C<sub>10</sub> haloalkyl with 1-10 halogens, C<sub>2</sub>-C<sub>8</sub> alkoxyalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl, C<sub>5</sub>-C<sub>10</sub> cycloalkenyl, or C<sub>6</sub>-C<sub>14</sub> cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>13</sup>, COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>13</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>13</sup>, NR<sup>16</sup>R<sup>15</sup>, CONR<sup>16</sup>R<sup>15</sup>, aryl, heteroaryl or heterocyclyl,  
 -aryl, aryl(C<sub>1</sub>-C<sub>4</sub> alkyl), heteroaryl, heteroaryl(C<sub>1</sub>-C<sub>4</sub> alkyl), heterocyclyl or heterocyclyl(C<sub>1</sub>-C<sub>4</sub> alkyl);

alternatively,  $\text{NR}^6\text{R}^7$  and  $\text{NR}^{6a}\text{R}^{7a}$  are independently piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3  $\text{C}_1$ - $\text{C}_4$  alkyl groups;

$\text{R}^8$  is independently selected at each occurrence from H or  $\text{C}_1$ - $\text{C}_4$  alkyl;

$\text{R}^9$  and  $\text{R}^{10}$  are independently selected at each occurrence from H,  $\text{C}_1$ - $\text{C}_4$  alkyl, or  $\text{C}_3$ - $\text{C}_6$  cycloalkyl;

$\text{R}^{11}$  is selected from H,  $\text{C}_1$ - $\text{C}_4$  alkyl,  $\text{C}_1$ - $\text{C}_4$  haloalkyl, or  $\text{C}_3$ - $\text{C}_6$  cycloalkyl;

$\text{R}^{12}$  is  $\text{C}_1$ - $\text{C}_4$  alkyl or  $\text{C}_1$ - $\text{C}_4$  haloalkyl;

$\text{R}^{13}$  is selected from  $\text{C}_1$ - $\text{C}_4$  alkyl,  $\text{C}_1$ - $\text{C}_4$  haloalkyl,  $\text{C}_2$ - $\text{C}_8$  alkoxyalkyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkyl,  $\text{C}_4$ - $\text{C}_{12}$  cycloalkylalkyl, aryl, aryl( $\text{C}_1$ - $\text{C}_4$  alkyl)-, heteroaryl or heteroaryl( $\text{C}_1$ - $\text{C}_4$  alkyl)-;

$\text{R}^{14}$  is selected from  $\text{C}_1$ - $\text{C}_{10}$  alkyl,  $\text{C}_3$ - $\text{C}_{10}$  alkenyl,  $\text{C}_3$ - $\text{C}_{10}$  alkynyl,  $\text{C}_3$ - $\text{C}_8$  cycloalkyl, or  $\text{C}_4$ - $\text{C}_{12}$  cycloalkylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkyl, halo,  $\text{C}_1$ - $\text{C}_4$  haloalkyl, cyano,  $\text{OR}^{15}$ ,  $\text{SH}$ ,  $\text{S}(\text{O})_n\text{R}^{15}$ ,  $\text{COR}^{15}$ ,  $\text{CO}_2\text{R}^{15}$ ,  $\text{OC}(\text{O})\text{R}^{15}$ ,  $\text{NR}^8\text{COR}^{15}$ ,  $\text{N}(\text{COR}^{15})_2$ ,  $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$ ,  $\text{NR}^8\text{CO}_2\text{R}^{15}$ ,  $\text{NR}^{16}\text{R}^{15}$ ,  $\text{CONR}^{16}\text{R}^{15}$ , and  $\text{C}_1$ - $\text{C}_6$  alkylthio,  $\text{C}_1$ - $\text{C}_6$  alkylsulfinyl and  $\text{C}_1$ - $\text{C}_6$  alkylsulfonyl;

$\text{R}^{15}$  and  $\text{R}^{16}$  are independently selected at each occurrence from H,  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_3$ - $\text{C}_{10}$  cycloalkyl,  $\text{C}_4$ - $\text{C}_{16}$  cycloalkylalkyl, except that for  $\text{S}(\text{O})_n\text{R}^{15}$ ,  $\text{R}^{15}$  cannot be H;

aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents independently selected at each occurrence from  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkyl, halo,  $\text{C}_1$ - $\text{C}_4$  haloalkyl, cyano,  $\text{OR}^{15}$ ,  $\text{SH}$ ,  $\text{S}(\text{O})_n\text{R}^{15}$ ,  $\text{COR}^{15}$ ,  $\text{CO}_2\text{R}^{15}$ ,  $\text{OC}(\text{O})\text{R}^{15}$ ,  $\text{NR}^8\text{COR}^{15}$ ,  $\text{N}(\text{COR}^{15})_2$ ,  $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$ ,  $\text{NR}^8\text{CO}_2\text{R}^{15}$ ,  $\text{NR}^{16}\text{R}^{15}$ , and  $\text{CONR}^{16}\text{R}^{15}$ ;

heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl,

thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>15</sup>, -COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>15</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>15</sup>, NR<sup>16</sup>R<sup>15</sup>, and CONR<sup>16</sup>R<sup>15</sup>;

heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>15</sup>, COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>15</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>15</sup>, NR<sup>15</sup>R<sup>16</sup>, and CONR<sup>16</sup>R<sup>15</sup>; and

n is independently at each occurrence 0, 1 or 2.